11-10-08

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DURE-312 DIV

"Express Mail" mailing label number EB 819 919 786 US I hereby certify that this document and referenced attachments are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR § 1.10, addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on 11/06/2008
By: Crystal Susa Printed: Crystal Susa

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Chen, et al.
Title: SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN MANAGEMENT
Serial No.: 10/699,521 **Filing date:** 10/31/2003
Examiner: SILVERMAN, Eric E. **Group Art Unit:** 1618

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Return Receipt Postcard;
2. Transmittal Fee Sheet (1pg.);
3. Request for Reconsideration of Holding of Abandonment under MPEP 711.03 (3pp.);
4. Copy of Office Action mailed 04/09/2008 (11pp.);
5. Copy of Response under 37 CFR 1.111, Transmittal Fee Sheet, Petition for Extension of Time, Statement under 37 CFR 3.73(b), copy of Return Receipt Postcard (28pp.);
6. Copy of stamped, return postcard (1pg.);
7. Copy Image File Wrapper from Public PAIR (2pp.).

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **53-1953.**

If there are any questions regarding the above, the Examiner is invited to call the undersigned at 408-777-4915.

Respectfully submitted,
DURECT CORPORATION

Date: 6 NOVEMBER 2008

Thomas P. McCracken
Reg. No. 38,548

2 Results Way
Cupertino, CA 95014
Fax: 408-777-3577

I hereby certify that this correspondence, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on 6 November 2008 in an envelope as "Express Mail Post Office to Addressee" service pursuant to 37 C.F.R. §1.10, Mailing Label Number EB 819919786US and addressed to: Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450.

Signature: Crystal Susa **Printed:** Crystal Susa

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	CHEN, et al.		
Title:	SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN MANAGEMENT		
Serial No.:	10/699,521	Filing Date:	31 October 2003
Examiner:	Silverman, Eric E.	Art Unit:	1618

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR RECONSIDERATION OF HOLDING OF ABANDONMENT UNDER M.P.E.P §711.03

Sir:

Applicants received a Notice of Abandonment for the above-identified patent application, which Notice was mailed on 27 October 2008. The Notice stated that no reply was received to the Office Action mailed on 9 April 2008.

Applicants respectfully request a withdrawal of the abandonment, in view of the evidence provided herein that a sufficient response was timely filed in reply to the said Office Action.

Attached hereto are the following evidentiary documents:

- A copy of the Office Action, mailed on 9 April 2008.

- A copy of Applicants' Response under 37 C.F.R. §1.111, submitted 9 October 2008, including an Amendment and Traversal (23 pages), a Transmittal Fee Sheet (2 pages), a Petition for Extension of Time (1 page), a Statement under 37 C.F.R. 3.73(b) (1 page), and a return postcard.

- A copy of the stamped return postcard, demonstrating receipt of Applicants' response by the USPTO on 14 October 2008.

- A copy of the Image File Wrapper from Public PAIR for USSN 10/699,521, showing processing of Applicants' response at the USPTO Mailroom and the matching of Applicants' response with the subject file.

In view of the above evidence, Applicants respectfully submit that a timely response was filed to the Office Action of 9 April 2008, and the basis for the Office's holding of abandonment is thus in error.

Withdrawal of the abandonment of the present application is therefore respectfully requested.

No Fees are believed to be due with the submission of this Request. However, the Commissioner is hereby authorized to charge any fees due under 37 C.F.R. §§ 1.16 and 1.17 that may be required by this Request, or to credit any overpayment, to Deposit Account No. **50-1953**.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious, and thus all claims are believed to be in proper condition for allowance. Acknowledgement of this status by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Office contemplates taking any action other than withdrawal of the abandonment of this application, Applicants request that the Office contacts the undersigned at (408) 777-4915.

Respectfully submitted,

Date: 6 November 2008

Thomas P. McCracken
Registration No. 38,548

For and on behalf of
DURECT CORPORATION
2 Results Way
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312 CIP

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,521	10/31/2003	Guohua Chen	ALZA-0129	4222

23377 7590 04/09/2008
WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

OIPE IAP18
NOV 06 2008
PATENT & TRADEMARK OFFICE

EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
04/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DOCKETED
Action: OA
Dates: 7/9/08 R F Due
R F Due
CD: 10/9/08 R F Due

Office Action Summary

Application No.	Applicant(s)	
10/699,521	CHEN ET AL.	
Examiner	**Art Unit**	
Eric E. Silverman, PhD	1618	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-122* is/are pending in the application.

4a) Of the above claim(s) *14-17,21,54-56 and 73-121* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-20,22-53,57-72 and 122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-3-06,2-9-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, filed 1/22/2007, is noted. Claims 1 - 122 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1 – 72 and 122, in the reply filed on 1/22/2007 is acknowledged. The traversal is on the ground(s) that the Office action does not give an appropriate explanation of the reason for serous burden. Applicant avers that the proffered explanation is merely a recitation of sections of the MPEP, and is not appropriate. This is not found persuasive because the explanation provided is considered appropriate according to current USPTO policies and procedures, and indeed the proffered explanation is currently a form paragraph approved for use by examiners as an explanation of burden in restriction requirements.

The requirement is still deemed proper and is therefore made **FINAL**.

Applicants' election of the polymer PLGA and the solvent benzyl alcohol as species of the invention is acknowledged. Because Applicants did not aver any error in the requirement for an election of species, and as such the election of species is being treated as an election **without traverse**. Applicants indicated that claims 1 - 13, 18 – 20, 22 – 53, 57 – 109, 11 [sic: 111] – 122 as readable on the elected species.

Accordingly claims 1 – 13, 18 – 20, 22 – 53, 57 – 72, and 122 are treated on the merits below, and claims 14 – 17, 21, 54 – 56, and 73 – 121 are withdrawn as reading on a non-elected invention or species.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 13, 18 – 20, 22 – 24, 28 – 39 and 122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 1, and 122 recite a "low molecular weight" polymer. Absent a definition in the specification, it is not clear what molecular weights are "low" as claimed. The artisan would thus be unable to determine the metes and bounds of the invention.

The remaining claims are rejected for ultimately depending on claim 1 without clarifying this issue.

Claim Rejections - 35 USC § 102

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 7, 10 – 12, 18 – 20, 22, 24,29 - 35, 40 - 52, 57 - 65, 70and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,130,200 to Brodbeck et al. of record

Claim 1 requires a sustained release dosage form, which is a gel comprising a low molecular weight bioerodibe polymer, a water-immiscible solvent in amount sufficient to form a gel with the polymer, and an anesthetic dissolved or dispersed in the gel.

The elected polymer is PLGA, and the elected solvent is benzyl alcohol.

Claims 2 - 4 relate to the efficacy ratio of claim 1's composition. It is understood that the composition of claim 1 would necessarily have these ratios. Claims 5 – 7 relate to the sustained release rate of claim 1. Claim 7 requires that sustained release last from about 24 hours to about 7 days. Claims 10 - 12 relate to the solvents of claim 1. Claim 10 requires a solvent having a miscibility in water less than 7 wt.% at 25C, and claim 11 forbids inclusion of any solvent having a greater miscibility. Claims 18 - 20 and 22 relate to the polymer, and read on the elected PLGA polymer. Claim 24 requires the polymer to have carboxylic acid end groups. It is understood that unmodified PLGA, being a polyester, has carboxylic acid end groups. Claims 25 - 28 relate to the polymers' molecular weight average molecular weight, with the most limiting claim (claim 28) requiring a molecular weight of about 5,000. Claims 29 – 31 relate to the amount of anesthetic, with claim 31 requiring the anesthetic to be present in about 1% to about 30% by weight. Claims 32 – 34 relate to the ratio of polymer and solvent, with claim 34 requiring the ratio to be between 30:70 and 75:25. Claim 35 requires an additional material, such as an excipient.

Claim 40 is similar to claim 1, but it additionally requires that the polymer be a lactic-acid based polymer, and that the weight average molecular weight be from about 3,000 to about 10,000. Claims 41 – 52, 57 – 65, and 72 are similar to the claims discussed above, except that they ultimately depend from claim 40 instead of claim 1.

Brodbeck teaches a composition that is a PLGA copolymer gel with a solvent present in amounts effective to plasticize the gel. Claim 1. The solvent has a miscibility in water of less than 7%. Claim 2. The solvent may be benzyl benzoate. Claim 3.

Benzyl benzoate is a recognized topical analgesic. See US 6,673,363 at claim 20. The sustained release, in some embodiements, occurs in a period of between about 24 hours and about 7 days. See Figure 2, plot with squares, and description thereof. When a mixture of solvents is used, such as 80/20 benzyl benzoate/triacetin or 80/20 benzyl benzoate/NMP, neither solvent has a miscibility in water of more than 7% by weight. See e.g. col. 13 lines 13 - 50. PLGA, being the elected polymer, is admitted to read on the polymer of instant claims 18, 19, and 22. Example 1 of the art shows 50:50 lactide:glycolide in the polymer, as per instant claim 20. As discussed above, when PLGA is not modified, it necessarily comprises carboxylic acid end groups, being a polyester. An exemplified PLGA molecular weight is 5,000. Col. 11, lines 23 – 41. The dosage form comprises, for example, 50% solvent and 50% polymer. Col. 14, lines 43 - 67. The solvent is, for example, 80:20 benzyl benzoate/triacetin. Col. 14, 43 - 67. As such the benzyl benzoate (anesthetic) is present in 40% of the final product by weight (50% product being solvent and 80% of the solvent being benzyl benzoate). 40% by weight reads on instant claims 29 - 30 literally, and is understood to be included in "about 30% by weight" recited in instant claim 31, because there is no specific definition of the limits of about, and the anesthetic would be expected to have the same or similar properties at 40% as at 30%. C.f. claim 20. Excipients, such as a component solvent that may be, for example, triacetin or NMP, are present in the composition of the art. Claims 16 – 19. A solubility modifier, pore former, emulsifier, or osmotic agent may also be present. Claims 4 – 7.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 – 7, 10 – 13, 18 – 20, 22 - 39, and 40 - 53, 57 - 72 and 122 rejected under 35 U.S.C. 103(a) as being unpatentable WO 238185 (185 or the 185 reference) of record, in view of US 6,432,415 to Osborne, of record.

The limitations of most of the claims have been discussed above.

Claim 13 ultimately depends on claim 1, and requires the solvent benzyl alcohol. Claim 53 ultimately depends on claim 40, and requires a benzyl alcohol.

Claims 36 - 39 require particular particle sizes of the active agent.

Claim 122 requires a kit, wherein the kit contains a gel vehicle comprising a low molecular weight bioerodibe polymer, a water-immiscible solvent in amount sufficient to

form a gel with the polymer, and an anesthetic dissolved or dispersed in the gel. One or more additional materials, such as an excipient, are also required. The kit requires that the anesthetic agent be separated from the solvent until the time of administration to the subject.

The 185 reference discloses an injectable gel composition that provides sustained release of an active at the site of injection. Examples. The polymer may be PLGA. Claim 4. The PLGA may have carboxylic acid end groups. Example 2. The solvent polymer ratio is commensurate with the instant claims. See Example 2 (45% by weight polymer in solvent). The solvent may be benzyl alcohol. Claim 7. The polymer may be a 50:50 lactide:glycolide polymer with a molecular weight of about 5,000. Example 2 (a molecular weight of 6,000 is about 5,000). The PLGA has either acid or ester end groups, or a mixture thereof, depending on the desired method of polymerization. Page 13. The system is readily injectable through a 20 gauge needle, and the beneficial agent, which is dispersed as particles. Examples 2 and 3. The composition may be a kit having the beneficial agent in a separate container from the other agents, such as the solvent. Claims 38 – 45. The excipient and solubility modifier polyethylene glycol, is added in some embodiments. Example 3. Delivery of the agent occurs, for example, over one or three days. Example 6.

What is lacking is:

1) A beneficial agent that is an anesthetic, and

2) The specific particle sizes of claims 36 – 39.

Osborne teaches gel forming compositions based on PLGA. Claims 1 and 8. Osborne suggests the use of an anesthetic in such compositions. Claim 5.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to incorporate an analgesic in the composition of 185. Doing so is merely following the suggestion of Osborne, who recognizes analgesics to be useful in similar compositions. The amount of anesthetic (instant claims 29 - 31 and 60 - 62) is a matter of dosing, which is routine optimization. It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to optimize the particle size. The particle size will clearly depend on the needle through which the composition of '185 needs to pass. Thus, the artisan will optimize the particle size to be large enough to be readily manufactured and handled, but small enough to pass through the desired needle.

Claims 1 – 13, 18 – 20, 22 – 53, 57 – 72, and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 238185 (185 or the 185 reference) of record, in view of US 6,432,415 to Osborne, as applied to claims 1 – 7, 10 – 13, 18 – 20, 22 - 39, and 40 - 53, 57 - 72 and 122 and in further view of US 5,614,206 to Randolph.

What is lacking from 185 and Osborne are the anesthetics of the instant claims, such as bipivacaine.

Randolph teaches that bipivacaine is an anesthetic suitable for formulation in a sustained release formulation. Claims 12, 20, and 26.

It would have been prima facie obvious to a person of ordinary skill in the art at the time of the invention to use bipivacaine as the drug in 185 and Osborne. Based on

the teachings of the art, the use of an anesthetic, particularly bipivacaine, in 185's composition is merely a combination of known elements leading to predictable results. The general composition of the claims is known, see 185 as applied above, but without anesthetics. Osborne shows that anesthetics are useful in related compositions, and suggests their use. Bipivacaine is an anesthetic. The Bipivacaine in the invention functions in the same way as in the art, namely by providing its recognized benefit. The dosage form carrying the bipivacaine also functions identically in the claims as in the art, namely by delivering an active in a sustained release manner. The combination gives no more than predictable results, and is therefore prime facie obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is (571)272-5549. The examiner can normally be reached on Monday to Thursday 7:00 am to 5:00 pm and Friday 7:00 am to noon.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571 272 0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Eric E Silverman, PhD/
Examiner, Art Unit 1618

Crystal Susa
DURECT CORPORATION
2 Results Way
Cupertino, CA 95014

MS Amendment
COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450

Mailed: 10/09/2008

Docket #: DURE-312 CON

Inventors: Chen, et al.
Title: SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN
Serial No.: 10/699,521 Filing Date: 10/31/2003

Enclosed:
_X_ Return Receipt Postcard;
_X_ Transmittal Sheet (2pp.);
X Petition for Extension of Time (1pg.);
X Response to Office Action (23pp);
X Statement under 3.73(b) (1pg.).

I hereby certify that this paper is being deposited with the United States Postal Service
As first class mail in an envelope addressed to:
MS Amendment , Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
on: 10/09/2008
Signature: Crystal Susa Printed: Crystal Susa

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Chen, et al.

Title: SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN
Serial No.: 10/699,521 **Filing date:** 10/31/2003
Examiner: Silverman, Eric E. **Group Art Unit:** 1618

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL FEE SHEET

Sir:

Transmitted herewith are the following for the above-identified application:

1. Return Receipt Postcard;
2. Transmittal Fee Sheet (2pp.);
3. Petition for Extension of Time (1pg.);
4. Response to Office Action (23pp.);
5. Statement under 37 CFR 3.73(b) (1pg.).

Fee Calculation – The fee has been calculated as follows:

CLAIMS AS FILED (Fees computed under §1.16)

Claims	Number Filed	Minus Claims previously paid for	Number Extra	Large Entity Rate	TOTAL
Claims	122	-122	0	X $ 50	$ 0
Independent Claims	1	-3	0	X $ 210	$ 0
Multiple Dependent Claim(s)			0	X $370	$ 0
Petition for 3 Month Extension of Time					$1050.00
				TOTAL:	**$1050.00**

Please charge Deposit Account No. **50-1953** in the amount of $ 1050.00 as set forth in this transmittal letter. The Commissioner is hereby authorized to charge any

additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953.**

If there are any questions regarding the above, the Examiner is invited to call the undersigned at 408-777-4915.

Respectfully submitted,
DIRECT CORPORATION

Date: 9 OCTOBER 2009

Thomas P. McCracken
Reg. No. 38,548

2 Results Way
Cupertino, CA 95014
Fax: 408-777-3577

Docket No.: DURE-312 CON

I hereby certify that this paper is being deposited with the United States Postal Service
As first class mail in an envelope addressed to:
MS Amendment , Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
on: 10/09/2008
Signature: Crystal Susa Printed: Crystal Susa

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Chen, et al.

Title: SUSTAINED RELEASE DOSAGE FORMS OF ANETHETICS FOR PAIN

Serial No.:	10/699,521	Filing Date:	10/31/2003
Examiner:	Silverman, Eric E.	Group Art Unit:	1618

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION FOR EXTENSION OF TIME

Sir:

Applicant respectfully petitions for a 3 -month extension of time within which to respond to the Office Action dated 04/09/2008, such extension allowing the undersigned until 10/09/2008 to respond.

Please charge Deposit Account No. **50-1953** in the amount of $ 1050.00 as set forth in the enclosed transmittal letter. The Commissioner is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. **50-1953.**

Respectfully submitted,
DURECT CORPORATION

Date: 9 October 2008

Thomas P. McCracken
Reg. No. 38,548

2 Results Way
Cupertino, CA 95014
Phone: (408)777-1417
Fax: (408)777-3577

I hereby certify that this correspondence, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on 9 October 2008 in an envelope with sufficient postage as First Class Mail service pursuant to 37 C.F.R. §1.8, and addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450 Alexandria, VA 22313-1450.

Signature: Crystal Susa Printed: Crystal Susa

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	CHEN, et al.		
Title:	SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN		
Serial No.:	10/699,521	Filing Date:	31 October 2003
Examiner:	Eric E. Silverman	Art Unit:	1618

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE UNDER 37 C.F.R. §1.111

Sir:

This paper is in response to the Office Action dated 9 April 2008 in the above-referenced application. Accordingly, a petition for a three-month extension of time, and the fee therefor accompany this response. Reconsideration of the application in light of the following amendments and accompanying remarks is respectfully requested.

CLAIM AMENDMENTS

1. (Currently Amended) A sustained release dosage form of an anesthetic comprising: a short duration gel vehicle comprising a low molecular weight bioerodible, biocompatible polymer and a water-immiscible solvent in an amount effective to plasticize the polymer and form a gel therewith; and an anesthetic dissolved or dispersed in the gel vehicle, wherein said anesthetic is selected from the group consisting of: bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine, and combinations thereof, and further wherein the dosage form provides for a reduced initial burst of the anesthetic from the dosage form after local administration.

2. (Original) The sustained release dosage form of claim 1 further comprising a controllable efficacy ratio to achieve a release profile.

3. (Original) The sustained release dosage form of claim 2 wherein the efficacy ratio is between about 1 and 200.

4. (Original) The sustained release dosage form of claim 3 wherein the efficacy ratio is between about 5 and 100.

5. (Original) The sustained release dosage form of claim 1 wherein the sustained release occurs in a period of less than or equal to about fourteen days.

6. (Original) The sustained release dosage form of claim 5 wherein the sustained release occurs in a period of less than or equal to about seven days.

7. (Original) The sustained release dosage form of claim 6 wherein the sustained release lasts for a period of between about 24 hours and about seven days.

8. (Currently Amended) The sustained release dosage form of claim 1 wherein the anesthetic is selected from the group consisting of: bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, ~~etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine,~~ and combinations thereof.

9. (Original) The sustained release dosage form of claim 1 wherein the anesthetic comprises bupivacaine.

10. (Original) The sustained release dosage form of claim 1 wherein the solvent has a miscibility in water of less than or equal to about 7 weight % at 25.degree. C.

11. (Original) The sustained release dosage form of claim 1 wherein the dosage form is free of solvents having a miscibility in water that is greater than 7 weight % at 25° C.

12. (Original) The sustained release dosage form of claim 1 wherein the solvent is selected from the group consisting of: an aromatic alcohol, lower alkyl esters of aryl acids, lower aralkyl esters of aryl acids, aryl ketones, aralkyl ketones, lower alkyl ketones, lower alkyl esters of citric acid, and combinations thereof.

13. (Original) The sustained release dosage form of claim 1 wherein the solvent comprises benzyl alcohol.

14. (Withdrawn) The sustained release dosage form of claim 1 wherein the solvent comprises benzyl benzoate.

15. (Withdrawn) The sustained release dosage form of claim 1 wherein the solvent comprises ethyl benzoate.

16. (Withdrawn) The sustained release dosage form of claim 1 wherein the solvent

comprises triacetin.

17. (Currently Amended) The sustained release dosage form of claim 1 ~~wherein the solvent comprises~~ further comprising a component solvent selected from the group consisting of: triacetin, diacetin, tributyrin, triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate, triethylglycerides, triethyl phosphate, diethyl phthalate, diethyl tartrate, mineral oil, polybutene, silicone fluid, glylcerin, ethylene glycol, polyethylene glycol, octanol, ethyl lactate, propylene glycol, propylene carbonate, ethylene carbonate, butyrolactone, ethylene oxide, propylene oxide, N-methyl-2-pyrrolidone, 2-pyrrolidone, glycerol formal, methyl acetate, ethyl acetate, methyl ethyl ketone, dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, caprolactam, decylmethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and combinations thereof.

18. (Original) The sustained release dosage form of claim 1 wherein the polymer comprises a lactic acid-based polymer.

19. (Original) The sustained release dosage form of claim 18 wherein the polymer comprises a copolymer of lactic acid and glycolic acid (PLGA).

20. (Original) The sustained release dosage form of claim 19 wherein the copolymer has a monomer ratio of lactic acid to glycolic acid of approximately 50:50.

21. (Withdrawn) The sustained release dosage form of claim 1 wherein the polymer comprises a caprolactone-based polymer.

22. (Original) The sustained release dosage form of claim 1 wherein the polymer is selected from the group consisting of: polylactides, polyglycolides, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene

terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof.

23. (Original) The sustained release dosage form of claim 19 wherein the polymer comprises an ester end group.

24. (Original) The sustained release dosage form of claim 19 wherein the polymer comprises a carboxylic acid end group.

25. (Original) The sustained release dosage form of claim 1 wherein the polymer has a weight average molecular weight of between about 3,000 and about 10,000.

26. (Original) The sustained release dosage form of claim 25 wherein the polymer has a weight average molecular weight of between about 3,000 and about 8,000.

27. (Original) The sustained release dosage form of claim 26 wherein the polymer has a weight average molecular weight of between about 4,000 and about 6,000.

28. (Original) The sustained release dosage form of claim 27 wherein the polymer has a weight average molecular weight of about 5,000.

29. (Original) The sustained release dosage form of claim 1 wherein the dosage form comprises from about 0.1% to about 50% anesthetic by weight.

30. (Original) The sustained release dosage form of claim 29 wherein the dosage form comprises from about 0.5% to about 40% anesthetic by weight.

31. (Original) The sustained release dosage form of claim 30 wherein the dosage

form comprises from about 1% to about 30% anesthetic by weight.

32. (Original) The sustained release dosage form of claim 1 wherein the ratio between the polymer and the solvent is between about 5:95 and about 90:10.

33. (Original) The sustained release dosage form of claim 32 wherein the ratio between the polymer and the solvent is between about 20:80 and about 80:20.

34. (Original) The sustained release dosage form of claim 33 wherein the ratio between the polymer and the solvent is between about 30:70 and about 75:25.

35. (Original) The sustained release dosage form of claim 1 further comprising at least one of the following: an excipient, an emulsifying agent, a pore former, a solubility modulator for the anesthetic, and an osmotic agent.

36. (Original) The sustained release dosage form of claim 1 wherein the anesthetic comprises particles having an average particle size of less than about 250 μm.

37. (Original) The sustained release dosage form of claim 36 wherein the anesthetic comprises particles having an average particle size of between about 5 μm and 250 μm.

38. (Original) The sustained release dosage form of claim 37 wherein the average particle size is between about 20 μm and about 125 μm.

39. (Original) The sustained release dosage form of claim 38 wherein the average particle size is between about 38 μm and about 63 μm.

40. (Original) A sustained release dosage form of an anesthetic comprising: a short duration gel vehicle comprising a low molecular weight lactic acid-based polymer

and a water-immiscible solvent, in an amount effective to plasticize the polymer and form a gel therewith; an anesthetic comprising bupivacaine, wherein the anesthetic is dissolved or dispersed in the gel vehicle; and a controllable efficacy ratio to achieve a release profile; wherein the weight average molecular weight of the lactic acid-based polymer is between about 3,000 and about 10,000.

41. (Original) The sustained release dosage form of claim 40 wherein the sustained release occurs in a period of less than or equal to about fourteen days.

42. (Original) The sustained release dosage form of claim 41 wherein the sustained release occurs in a period of less than or equal to about seven days.

43. (Original) The sustained release dosage form of claim 42 wherein the sustained release lasts for a period of between about 24 hours and about seven days.

44. (Original) The sustained release dosage form of claim 40 wherein the efficacy ratio is between about 1 and about 200.

45. (Original) The sustained release dosage form of claim 44 wherein the efficacy ratio is between about 5 and about 100.

46. (Original) The sustained release dosage form of claim 40 wherein the polymer comprises a copolymer of lactic acid and glycolic acid (PLGA).

47. (Original) The sustained release dosage form of claim 46 wherein the copolymer has a monomer ratio of lactic acid to glycolic acid of approximately 50:50.

48. (Original) The sustained release dosage form of claim 46 wherein the copolymer comprises poly(D,L-lactide-co-glycolide).

49. (Original) The sustained release dosage form of claim 46 wherein the copolymer comprises poly(L-lactide-co-glycolide).

50. (Original) The sustained release dosage form of claim 40 wherein the solvent has a miscibility in water of less than or equal to about 7 weight % at 25°C.

51. (Original) The sustained release dosage form of claim 40 wherein the dosage form is free of solvents having a miscibility in water that is greater than 7 weight % at 25°C.

52. (Original) The sustained release dosage form of claim 40 wherein the solvent is selected from the group consisting of: an aromatic alcohol, lower alkyl esters of aryl acids, lower aralkyl esters of aryl acids; aryl ketones, aralkyl ketones, lower alkyl ketones, lower alkyl esters of citric acid, and combinations thereof.

53. (Original) The sustained release dosage form of claim 40 wherein the solvent comprises benzyl alcohol.

54. (Withdrawn) The sustained release dosage form of claim 40 wherein the solvent comprises benzyl benzoate.

55. (Withdrawn) The sustained release dosage form of claim 40 wherein the solvent comprises ethyl benzoate.

56. (Withdrawn) The sustained release dosage form of claim 40 wherein the solvent comprises triacetin.

57. (Original) The sustained release dosage form of claim 40 wherein the polymer has a weight average molecular weight of between about 3,000 and 8,000.

58. (Original) The sustained release dosage form of claim 57 wherein the polymer has a weight average molecular weight of between about 4,000 and 6,000.

59. (Original) The sustained release dosage form of claim 58 wherein the polymer has a weight average molecular weight of about 5,000.

60. (Original) The sustained release dosage form of claim 40 wherein the dosage form comprises from about 0.1% to about 50% anesthetic by weight.

61. (Original) The sustained release dosage form of claim 60 wherein the dosage form comprises from about 0.5% to about 40% anesthetic by weight.

62. (Original) The sustained release dosage form of claim 61 wherein the dosage form comprises from about 1% to about 30% anesthetic by weight.

63. (Original) The sustained release dosage form of claim 62 wherein the ratio between the polymer and the solvent is between about 5:95 and about 90:10.

64. (Original) The sustained release dosage form of claim 63 wherein the ratio between the polymer and the solvent is between about 20:80 and about 80:20.

65. (Original) The sustained release dosage form of claim 64 wherein the ratio between the polymer and the solvent is between about 30:70 and about 75:25.

66. (Original) The sustained release dosage form of claim 40 wherein the anesthetic comprises particles having an average particle size of less than about 250 μm.

67. (Original) The sustained release dosage form of claim 66 wherein the anesthetic comprises particles having an average particle size of between about 5 μm and about 250 μm.

68. (Original) The sustained release dosage form of claim 67 wherein the average particle size is between about 20 μm and about 125 μm.

69. (Original) The sustained release dosage form of claim 68 wherein the average particle size is between about 38 μm and about 63 μm.

70. (Original) The sustained release dosage form of claim 46 wherein the PLGA comprises an ester end group.

71. (Original) The sustained release dosage form of claim 46 wherein the PLGA comprises a carboxyl end group.

72. (Original) The sustained release dosage form of claim 40 further comprising at least one of the following: an excipient, an emulsifying agent, a pore former, a solubility modulator for the anesthetic, and an osmotic agent.

73. (Withdrawn) A method of treating local pain of a subject using a sustained release dosage form, the method comprising: administering a short duration sustained release dosage form comprising a gel vehicle, which comprises a low molecular weight bioerodible, biocompatible polymer, and a water-immiscible solvent in an amount effective to plasticize the polymer and form a gel therewith; and an anesthetic dissolved or dispersed in the gel vehicle.

74. (Withdrawn) The method of claim 73 wherein the sustained release dosage form further comprises a controllable efficacy ratio to achieve a release profile.

75. (Withdrawn) The method of claim 74 wherein the efficacy ratio is between about 1 and 200.

76. (Withdrawn) The method of claim 75 wherein the efficacy ratio is between about 5 and 100.

77. (Withdrawn) The method of claim 73 wherein the sustained release occurs in a period of less than or equal to about fourteen days.

78. (Withdrawn) The method of claim 77 wherein the sustained release occurs in a period of less than or equal to about seven days.

79. (Withdrawn) The method of claim 78 wherein the sustained release lasts for a period of between about 24 hours and about seven days.

80. (Withdrawn) The method of claim 73 further comprising administering the dosage form once.

81. (Withdrawn) The method of claim 73 further comprising applying the dosage form topically to the local pain.

82. (Withdrawn) The method of claim 73 further comprising injecting the dosage form at a location near the local pain.

83. (Withdrawn) The method of claim 73 further comprising delivering the anesthetic systemically.

84. (Withdrawn) The method of claim 73 further comprising delivering the anesthetic to multiple sites.

85. (Withdrawn) The method of claim 84 further comprising delivering injecting the dosage form at multiple locations surrounding the local pain.

86. (Withdrawn) The method of claim 73 further comprising repeating the administration of the dosage form.

87. (Withdrawn) The method of claim 73 wherein the anesthetic is selected from the group consisting of: bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine, and combinations thereof.

88. (Withdrawn) The method of claim 73 wherein the anesthetic comprises bupivacaine.

89. (Withdrawn) The method of claim 73 wherein the has a miscibility in water of less than or equal to about 7 weight % at 25°C.

90. (Withdrawn) The method of claim 73 wherein the polymer has a molecular weight of between about 3,000 and 10,000.

91. (Withdrawn) The method of claim 90 wherein the polymer has a weight average molecular weight of between about 3,000 and 8,000.

92. (Withdrawn) The method of claim 91 wherein the polymer has a weight average molecular weight of between about 4,000 and 6,000.

93. (Withdrawn) The method of claim 92 wherein the polymer has a weight average molecular weight of about 5,000.

94. (Withdrawn) The method of claim 73 wherein the dosage form comprises from about 0.1 to about 50% anesthetic by weight.

95. (Withdrawn) The method of claim 73 wherein the polymer is selected from the

group consisting of: polylactides, polyglycolides, poly(caprolactone), polyanhydrides, polyamines, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyphosphoesters, polyesters, polybutylene terephthalate, polyorthocarbonates, polyphosphazenes, succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, polysaccharides, chitin, chitosan, hyaluronic acid, and copolymers, terpolymers and mixtures thereof.

96. (Withdrawn) The method of claim 73 wherein the sustained release dosage form comprises a ratio of about 5:95 and about 90:10 between the polymer and the solvent.

97. (Withdrawn) The method of claim 73 wherein the anesthetic comprises particles having an average particle size of less than about 250 μm.

98. (Withdrawn) A method of treating post-surgical local pain of a subject using a sustained release dosage form, the method comprising: administering once a short duration sustained release dosage form comprising a gel vehicle, which comprises a low molecular weight bioerodible, biocompatible lactic acid-based polymer, and a water-immiscible solvent in an amount effective to plasticize the polymer and form a gel therewith; an anesthetic comprising bupivacaine dissolved or dispersed in the gel vehicle; and a controllable efficacy ratio to achieve a release profile.

99. (Withdrawn) The method of claim 98 wherein the polymer comprises a copolymer of lactic acid and glycolic acid (PLGA).

100. (Withdrawn) The method of claim 99 wherein the copolymer has a monomer ratio of lactic acid to glycolic acid of approximately 50:50.

101. (Withdrawn) A method of preparing a sustained release dosage form, the method comprising: preparing a short duration gel vehicle comprising a low molecular weight bioerodible, biocompatible polymer and a water-immiscible solvent in an amount

effective to plasticize the polymer and form a gel therewith to create a polymer/solvent solution or gel; equilibrating the polymer/solvent mixture until a clear homogeneous solution or gel is achieved; dissolving or dispersing an anesthetic into the polymer/solvent solution or gel; blending the anesthetic and the polymer/solvent solution or gel to form a sustained release dosage form; and controlling an efficacy ratio to achieve a release profile.

102. (Withdrawn) The method of claim 101 wherein the efficacy ratio is between about 1 and 200.

103. (Withdrawn) The method of claim 101 wherein the polymer/solvent solution or gel is equilibrated at a temperature between room temperature and approximately 65°C.

104. (Withdrawn) The method of claim 101 wherein the anesthetic comprises bupivacaine.

105. (Withdrawn) The method of claim 101 wherein the anesthetic is selected from the group consisting of: bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine, and combinations thereof.

106. (Withdrawn) The method of claim 101 wherein the polymer comprises a lactic acid-based polymer.

107. (Withdrawn) The method of claim 106 wherein the polymer comprises a copolymer of lactic acid and glycolic acid (PLGA).

108. (Withdrawn) The method of claim 107 wherein the copolymer has a monomer ratio of lactic acid to glycolic acid of approximately 50:50.

109. (Withdrawn) The method of claim 107 wherein the polymer comprises poly(D,L-lactide-co-glycolide).

110. (Withdrawn) The method of claim 107 wherein the polymer comprises poly(L-lactide-co-glycolide).

111. (Withdrawn) The method of claim 101 comprising loading the dosage form with from about 0.1% to about 50% anesthetic by weight of the dosage form.

112. (Withdrawn) The method of claim 111 comprising loading the dosage form with from about 0.5% to about 40% anesthetic by weight of the dosage form.

113. (Withdrawn) The method of claim 112 comprising loading the dosage form with from about 1% to about 30% anesthetic by weight of the dosage form.

114. (Withdrawn) The method of claim 101 comprising providing a ratio of about 5:95 and about 90:10 between the polymer and the solvent.

115. (Withdrawn) The method of claim 114 comprising providing a ratio of about 20:80 and about 80:20 between the polymer and the solvent.

116. (Withdrawn) The method of claim 115 comprising providing a ratio of about 30:70 and about 75:25 between the polymer and the solvent.

117. (Withdrawn) The method of claim 101 wherein the solvent is selected from the group consisting of: an aromatic alcohol, lower alkyl esters of aryl acids, lower aralkyl esters of aryl acids; aryl ketones, aralkyl ketones, lower alkyl ketones, lower alkyl esters of citric acid, and combinations thereof.

118. (Withdrawn) The method of claim 107 wherein the PLGA comprises an ester

end group.

119. (Withdrawn) The method of claim 107 wherein the PLGA comprises a carboxyl end group.

120. (Withdrawn) The method of claim 101 further comprising adding at least one of the following to the dosage form: an excipient, an emulsifying agent, a pore former, a solubility modulator for the anesthetic, and an osmotic agent.

121. (Withdrawn) The method of claim 101 wherein the anesthetic comprises particles having an average particle size of less than about 250 μm.

122. (Original) A kit for administration of a sustained delivery of an anesthetic to local pain of a subject comprising: a short duration gel vehicle comprising a low molecular weight bioerodible, biocompatible polymer and a water-immiscible solvent, in an amount effective to plasticize the polymer and form a gel therewith; an anesthetic dissolved or dispersed in the gel vehicle; and optionally, one or more of the following: an excipient; an emulsifying agent; a pore former; a solubility modulator for the anesthetic, optionally associated with the anesthetic; and an osmotic agent; wherein at the least anesthetic agent, optionally associated with the solubility modulator, is maintained separated from the solvent until the time of administration of the anesthetic to the subject.

REMARKS

Status of the Claims

Claims 1-122 are pending in the application.

Claims 14-17, 21, 54-56 and 73-121 have been withdrawn pursuant to 37 C.F.R. §1.142.

Claims 1 and 8 have been amended by entry of this amendment.

Claim 17 has been reasserted and amended by entry of this amendment.

Claims 1-13, 17-20, 22-53, 57-72 and 122 remain under consideration with entry of this amendment.

Summary

Claims 1-13, 18-20, 22-53, 57-72 and 122 are pending in the application and were examined in the Office Action dated 9 April 2008. In the subject Office Action, the following claim rejections have been raised: **(a)** claims 1-13, 18-20, 22-24, 28-39 and 122 were rejected under 35 U.S.C. §112, second paragraph, on the basis of clarity; **(b)** claims 1-7, 10-12, 18-20, 22, 24, 29-35, 40-52, 57-65, 70 and 72 were rejected under 35 U.S.C. §102(b) as unpatentable over U.S. Patent No. 6,130,200 to Brodbeck et al. ("Brodbeck"); **(c)** claims 1-7, 10-13, 18-20, 22-39, 40-53, 57-72 and 122 were rejected under 35 U.S.C. §103(a) as unpatentable over International Publication No. WO 02/38185 to Dunn et al. ("Dunn") in view of U.S. Patent No. 6,432,415 to Osborne et al. ("Osborne"); and **(d)** claims 1-13, 18-20, 22-53, 57-72 and 122 were rejected under 35 U.S.C. §103(a) as unpatentable over Dunn in view of Osborne and in further view of U.S. Patent No. 5,614,206 to Randolph et al. ("Randolph"). Applicants respectfully traverse all pending claim rejections for the following reasons.

Overview of the Amendments

Applicants, by way of this Response, have re-entered claim 17 for consideration on the merits. In addition, applicants have amended claims 1, 8 and 17 in order to recite

the invention with greater particularity. More specifically, claim 1 has been amended to recite specific anesthetic agents that are included in the claimed compositions. Support for this amendment can be found throughout the specification and claims as originally filed, and in particular in claim 8 and in the specification at Paragraphs [0013], [0082], and [0089], and in the working examples. In addition, claim 1 has been amended to recite that the dosage form provides for a reduced initial bust after local administration. Support for this amendment can be found in the specification at Paragraphs [0086] and [0087]. Claim 8 has been amended to further limit the selection of anesthetics in light of the amendments to the base claim (claim 1). Claim 17 has been amended to more clearly recite that the "component solvent" is an additional element to the base (claim 1) composition. Support for this amendment can be found throughout the specification as originally filed, in particular at Paragraphs [0043], [0083] and [0084]. Accordingly, no new matter has been added by way of the amendments to claims 1, 8 and 17, and the entry thereof is respectfully requested.

The Election/Restriction under 35 U.S.C. §1.121

The Office has withdrawn claim 17 from consideration on the merits on the basis that the claim reads on a non-elected invention or species. Applicants traverse the withdrawal on the following basis.

Claim 17 as originally filed recites the composition of claim 1 comprising "a component solvent" selected from a group of recited solvents. Applicants refer the Office's attention to the specification, Paragraph [0043] at the top of page 8, line 4, wherein "component solvents" are defined as an optional addition to the base composition that contains the water-immiscible solvent. In addition, in Paragraphs [0083] and [0084], pages 16-17 of the specification, applicants further disclose the addition of such optional "component solvents" to the base formulation that includes the water-immiscible solvent that was the subject of the species election. Accordingly, the election of the water-immiscible solvent species (benzyl alcohol) has no preclusive effect with respect to the subject matter of claim 17, as that claim is still readable upon the elected species. Applicants therefore respectfully request that the Office re-enter claim

17 and examine that claim on the merits. Finally, applicants draw the Office's attention to the amendment made to claim 17 by way of this Response. As can be seen, the amendment clarifies that the "component solvent" is a further constituent of the bases composition of claim 1.

The Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1-13, 18-20, 22-24, 28-39 and 122 stand rejected under 35 U.S.C. §112, second paragraph, as indefinite. In particular, the Office has objected that applicants' recitation of a "low molecular weight" polymer in base claims 1 and 122 is indefinite, on the basis that "[a]bsent a definition in the specification, it is not clear what molecular weights are 'low' as claimed." Office Action at page 3. Applicants respectfully traverse the rejection.

In assessing a claim for compliance with 35 U.S.C. §112, second paragraph, one must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope, therefore providing the notice function of 35 U.S.C. §112, second paragraph. See *Solomon v. Kimberly-Clark Corp.*, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). In providing this notice function, a patent applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claims that make clear the boundaries of the subject matter for which protection is sought. In fact, a claim may not be rejected solely on the basis of the type of language used to define the subject matter for which patent protection is sought. *In re Swinehart*, 160 USPQ 226 (CCPA 1971). Further, the meaning of a claim term need only be apparent from the prior art or from the specification and drawings at the time an application is filed. In this regard, applicants need not confine themselves to the terminology used in the prior art; however, applicants are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention may be ascertained. See, e.g., *In re Morris*, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997) and *In re Prater*, 162 USPQ 541 (CCPA 1969).

In base claims 1 and 122, applicants have used the term "low molecular weight" to describe the selected polymer for use in the recited compositions. In the specification

as originally filed, applicants have provided a clear and precise definition for the term "low molecular weight polymer" that includes a specific overall weight average molecular weight range and a series of preferred sub-ranges, as well as the precise test that can be used to ascertain such molecular weight values. See Paragraph [0059], at page 11 of applicants' specification. The definition further provides precise chemical/physical feature of the selected low molecular weight polymer by requiring that that polymer is bioerodible. Applicants respectfully submit that their specification and claims therefore more than adequately apprise one of ordinary skill in the art the entire scope of the claimed invention, therefore satisfying the notice function of 35 U.S.C. §112, second paragraph. Reconsideration and withdrawal of the rejection of claims 1-13, 18-20, 22-24, 28-39 and 122 under 35 U.S.C. §112, second paragraph, is thus earnestly solicited.

The Rejection under 35 U.S.C. §102(b)

Claims 1-7, 10-12, 18-20, 22, 24, 29-35, 40-52, 57-65, 70 and 72 stand rejected under 35 U.S.C. §102(b) as anticipated by Brodbeck. Applicants respectfully traverse the rejection for the following reasons.

Applicants draw the Office's attention to the amendment to claim 1, wherein the anesthetic must be selected from the group consisting of: bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine, and combinations thereof. The Office has noted Brodbeck's disclosure of benzyl benzoate as the solvent (or use of benzyl benzoate in a combination of solvents) that can be used to form a gel vehicle that is then used to carry and release an additional component (an agent of interest that is intended for sustained release from the gel vehicle), and argues that benzyl benzoate is recognized as a topical anesthetic. Office Action at pages 4-5. Applicants respectfully traverse the rejection on the basis that due to the amendment to claim 1, all rejected claims now require selection from a list of specified long-acting anesthetics that excludes the benzyl benzoate solvent. Reconsideration and withdrawal of the rejection of claims

1-7, 10-12, 18-20, 22, 24, 29-35, 40-52, 57-65, 70 and 72 under 35 U.S.C. §102(b) is thus earnestly solicited.

The Rejections under 35 U.S.C. §103(a)

Claims 1-7, 10-13, 18-20, 22-39, 40-53, 57-72 and 122 stand rejected under 35 U.S.C. §103(a) as obvious over Dunn in view of Osborne. In particular, the Office asserts that the primary reference to Dunn describes a few of the components of applicants' recited compositions (a polymer and a solvent), but acknowledges that there are missing elements (a beneficial agent that is an anesthetic, and the specific particles sizes recited in claims 36-39). Office Action at pages 6-7. The Office attempts to overcome the missing disclosure from Dunn by looking to the secondary reference to Osborne which includes "local anesthetics" in a long laundry list of active agents. Office Action at page 8. The Office then asserts that selection of particle sizes "is routine optimization" and "clearly depends upon the needle through which the composition of Dunn needs to pass." Office Action at page 8. Applicants respectfully traverse the rejection.

The Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a). *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). According to the Federal Circuit, "the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so." *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007).

With regard to the Office's proposed combination as compared to applicants' original claims, the Office has failed to identify from its Dunn/Osborne combination dosage forms having a controllable efficacy ratio and/or efficacy ratios of 1-200 or 5-100 (see applicants' claims 2-4). With regard to applicants' recited particle sizes (for suspension formulations), applicants respectfully note that their specified particles sizes (250 μm, 5-250 μm, 20-125 μm and 38-63 μm) are unrelated to any concern about the ability to administer a formulation through a particular needle size since the recited

micron size ranges are orders of magnitude less than the smallest possible internal diameter of medical needles which very quickly approach millimeter sizes in lower gauge systems. Furthermore, with respect to the claims as now amended, the proposed Dunn/Osborne combination is also missing the following recited elements: **(a)** a long acting anesthetic selected from bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-etidocaine, dextro-etidocaine, levo-mepivacaine, and combinations thereof; and **(b)** a reduced initial burst after local administration.

Applicants have disclosed and claimed new and useful anesthetic dosage forms that have an improved delivery performance (for example as evidenced with the tight control over delivery efficacy ratios), and at the same time enhanced safety profiles (the ability to reduce initial burst avoids potential harmful side effects from too much anesthetic being delivered in the first 24 hours of administration. The Office's proposed combination of Dunn and Osborne fails to establish that applicants' recited compositions were obvious. In addition, since the recited compositions were neither taught nor suggested by the Dunn/Osborne combination, it cannot be argued that the skilled person would have had a reasonable expectation of success in making those specific compositions. In other words, the Office's proposed combination of Dunn and Osborne fails to establish a *prima facie* case of obviousness of applicants' claimed compositions. Reconsideration and withdrawal of the rejection of claims 1-7, 10-13, 18-20, 22-39, 40-53, 57-72 and 122 under 35 U.S.C. §103(a) is thus earnestly solicited.

Claims 1-13, 18-20, 22-53, 57-72 and 122 stand rejected under 35 U.S.C. §103(a) as unpatentable over the combination of Dunn in view of Osborne and in further view of Randolph. The Office recites the same combination of Dunn and Osborne as discussed herein above, and then adds Randolph on the basis that it "teaches that bupivacaine is an anesthetic suitable for formulation in a sustained release formulation." Office Action at page 8. Applicants respectfully traverse the rejection for the following reasons.

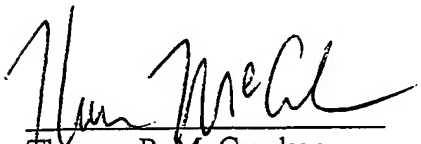
The failure of the Office's base combination (Dunn/Osborne) to render obvious applicants' recited compositions has been established above. In particular, applicants have disclosed and claimed new and useful anesthetic dosage formulations that have an

improved delivery performance (for example as evidenced with the tight control over delivery efficacy ratios), and at the same time has enhanced safety profiles (the ability to reduce initial burst avoids potential harmful side effects from too much anesthetic being delivered in the first 24 hours of administration). The addition of Randolph to this basic combination also fails to establish a *prima facie* case of obviousness of applicants' claimed compositions. This is because the specified performance requirements of applicants' recited compositions cannot be derived from Dunn/Osborne/Randolph when those references are considered alone or in any conceivable combination. Reconsideration and withdrawal of the rejection of claims 1-13, 18-20, 22-53, 57-72 and 122 under 35 U.S.C. §103(a) is thus earnestly solicited.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

Respectfully submitted,



Date: 9 October 2008

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PTO/SB/96 (09-08)
Approved for use through 10/31/2008. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

STATEMENT UNDER 37 CFR 3.73(b)

Applicant/Patent Owner: Durect Corporation

Application No./Patent No.: 10/699,521 Filed/Issue Date: 10/31/2003

Entitled: SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN

Durect (Name of Assignee), a Corporation (Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that it is:

1. ☑ the assignee of the entire right, title, and interest; or
2. ☐ an assignee of less than the entire right, title and interest
(The extent (by percentage) of its ownership interest is _____ %)

in the patent application/patent identified above by virtue of either:

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[NOTE: A separate copy (*i.e.*, a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Signature	10/09/2008 Date
Thomas P. McCracken Printed or Typed Name	4087771417 Telephone Number
Vice President, Chief Patent Counsel, Durect Corporation Title	

MS Amendment
COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450

Mailed:10/09/2008

Docket #: DURE-312 CON

Inventors: Chen, et al.
Title: SUSTAINED RELEASE DOSAGE FORMS OF ANESTHETICS FOR PAIN
Serial No.: 10/699,521 Filing Date: 10/31/2003

Enclosed:
_X_ Return Receipt ~~Postcard~~;
_X_ Transmittal Sheet (2pp.);
_X_ Petition for Extension of Time (1pg.);
_X_ Response to Office Action (23pp);
_X_ Statement under 3.73(b) (1pg.).

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10/699,521 Sustained release dosage forms of anesthetics for pain management

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